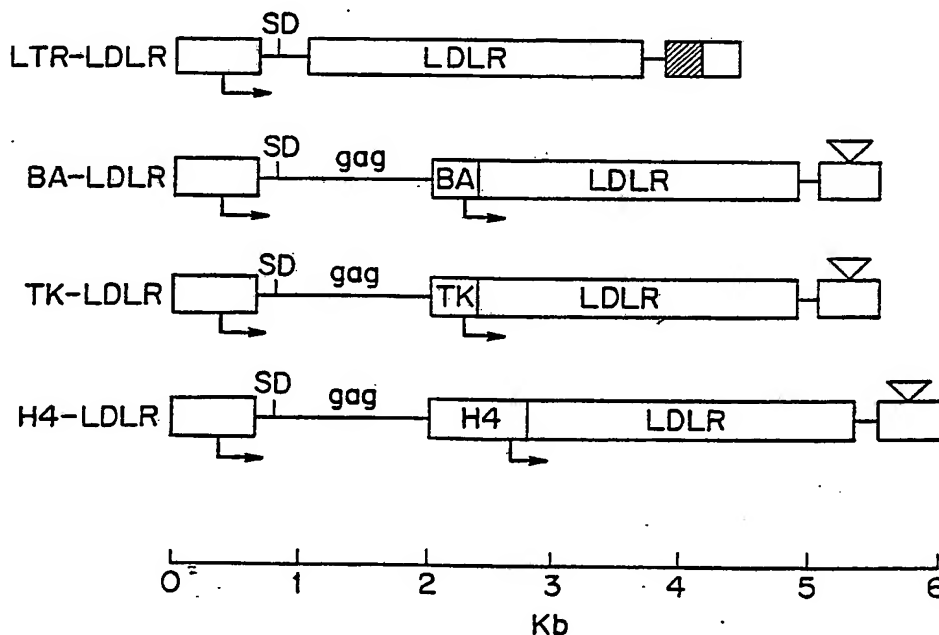




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(21) International Application Number: PCT/US89/00422 (22) International Filing Date: 2 February 1989 (02.02.89) (31) Priority Application Number: 152,749 (32) Priority Date: 5 February 1988 (05.02.88) (33) Priority Country: US (71) Applicants: WHITEHEAD INSTITUTE FOR BIOMEDICAL RESEARCH [US/US]; Nine Cambridge Center, Cambridge, MA 02142 (US). HOWARD HUGHES MEDICAL INSTITUTE [US/US]; 6701 Rockledge Drive, Bethesda, MD 20817 (US). (72) Inventors: WILSON, James, M. ; 24 Whitman Road, Waltham, MA 02154 (US). MULLIGAN, Richard, C. ; 441 Franklin Street, Cambridge, MA 02138 (US).	(74) Agents: GRANAHAH, Patricia et al.; Hamilton, Brook, Smith & Reynolds, Two Militia Drive, Lexington, MA 02173 (US). (81) Designated States: AT (European patent), BE (European patent), CH (European patent), DE (European patent), FR (European patent), GB (European patent), IT (European patent), JP, LU (European patent), NL (European patent), SE (European patent). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 24 August 1989 (24.08.89)	

(54) Title: MODIFIED HEPATOCYTES AND USES THEREFOR



(57) Abstract

Genetically engineered or transduced hepatocytes which express genetic material of interest introduced or incorporated into them, as well as methods of producing, transplanting and using the genetically engineered hepatocytes. The genetic material of interest can be incorporated through use of a vector, such as a recombinant retrovirus, which contains the genetic material of interest, or by other means.

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INTERNATIONAL SEARCH REPORT

International Application No PCT/US 89/00422

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) *		
According to International Patent Classification (IPC) or to both National Classification and IPC		
IPC ⁴ : C 12 N 5/00; C 12 N 15/00		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
IPC ⁴	C 12 N	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched *		
III. DOCUMENTS CONSIDERED TO BE RELEVANT *		
Category *	Citation of Document, ¹¹ with Indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
X	Proc. Natl. Acad. Sci. USA, vol. 84, May 1987, J.A. Wolff et al.: "Expression of retrovirally transduced genes in primary cultures of adult rat hepatocytes", pages 3344-3348 see the whole article --	1-8,11-13, 15-18,27
X	Proc. Natl. Acad. Sci. USA, vol. 81, October 1984, H.C. Isom et al.: "Quantitative assay for albumin-producing liver cells after simian virus 40 transformation of rat hepatocytes maintained in chemically defined medium", pages 6378-6382 see the whole article --	1-6
./.		
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>* Special categories of cited documents: ¹⁰</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified).</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means.</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"A" document member of the same patent family</p> </div> </div>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	
19th May 1989	25. 07. 89	
International Searching Authority	Signature of Authorized Officer	
EUROPEAN PATENT OFFICE	 P.C.G. VAN DER PIJPEN	

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

X,P	Proc. Natl. Acad. Sci. USA, vol. 85, June 1988, J.M. Wilson et al.: "Correction of the genetic defect in hepatocytes from the Watanabe heritable hyperlipidemic rabbit", pages 4421-4425 see the whole article -----	1-8,11-18, 27
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V. ☒ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE ¹

This International search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. ☒ Claim numbers 19-26 because they relate to subject matter not required to be searched by this Authority, namely:

See PCT Rule 39.1 (iv)

Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.

2. ☐ Claim numbers _____, because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim numbers _____, because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).

VI. ☐ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING ²

This International Searching Authority found multiple inventions in this international application as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.
2. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:
3. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:
4. ☐ As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

- ☐ The additional search fees were accompanied by applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.